Claim 5 is amended for better consistency with the claims from which it depends. This amendment is not made for reasons related to patentability. Entry of the amendment is respectfully requested.

Claims 1-7 and 12-20 were rejected under 35 U.S.C. Section 103(a) as allegedly being obvious over Wu *et al.* (U.S. Patent No. 5,452,723). Because the claimed systems and methods are in no way shown or suggested by Wu *et al.*, Applicants traverse this rejection.

First, the subject patent application discloses a system and method for determining optical characteristics such as the absorption coefficient μ_a, the reduced scattering coefficient $\mu_{s'}$ and a parameter γ from the spatially resolved reflectance $R(\rho)$. This determination involves, among other things, the dependence of the diffuse reflectance R on the distance ρ separating the source of illumination and the optical detector. This dependence of R on ρ does not at all appear in Wu *et al.* The diffuse reflectance $R(\mu_a,\mu_s,g)$ of Wu *et al.* is a value of the reflectance integrated over space and does not contain any information on its dependence on the source-detector distance ρ. Because Wu *et al.* does not disclose or suggest measuring the spatially resolved reflectance as set forth in claim 1, Wu *et al.* cannot render obvious this claim or the claims that refer back thereto. A

Second, the parameter γ proposed in the subject patent application and specified in claim 1 is a new concept which cannot be related simply to g and g' appearing in equation 13 of Wu *et al.*: k(g')/k(g)= 1-g'/1-g. In particular, g' cannot be written g_2. The first and second moment, g_1 and g_2, of the phase function $p(\theta)$ should not be confused with the first two terms of the Legendre polynomial expansion of the phase function,

which are mentioned in col. 8, line 8 of Wu *et al.* These first two terms are in this case the moment of order zero g_0, which is equal to 1, and the first moment (moment of order one) which is equal to the anisotropy factor g. *See* Wu *et al.*, col 6, line 66. The second moment g_2 (moment of order 2) corresponds to the third term of the Legendre polynomial expansion of the phase function. This second moment g_2 is never mentioned by Wu *et al.* In other words, Wu *et al.* assume that the ***total reflectance*** $R(\mu_a,\mu_s,\gamma)$ depends on the first moment of the phase function $g_1=g$ (corresponding to the second term of the Legendre expansion, the first term being a normalization factor). In complete contradistinction, the subject patent application shows that the *spatially-resolved reflectance* $R(\rho\ \mu_a,\mu_s,\gamma)$ depends on both the first and second moments of the phase function g_1 and g_2 (corresponding to the second and third term of the Legendre expansion). The approach of the subject application is fundamentally different and cannot be derived from Wu *et al.*'s approach. For these additional reasons, Wu *et al.* cannot render obvious the subject matter of claims 1-7 and 12-20. A ?

Third, the methodology used by Wu *et al.* is quite different than that described in the subject application. In particular, Wu *et al.* discloses a method to determine reflectance as a function of certain optical characteristics. In contrast, the claimed systems and method determine certain optical characteristics from reflectance. For these still further reasons, Wu *et al.* cannot render obvious the subject matter of claims 1-7 and 12-20. A ?

New claims 21-41 have been added for the Examiner's consideration. The subject matter of these new claims is fully supported by the original disclosure and no new matter is added. Applicants respectfully submit that the subject matter of new

claims 21-41 is not taught or suggested by the applied art. For example, the applied art does not teach or suggest a phase function parameter that depends on the first and second moments of a polynomial expansion of the phase function.

Applicants respectfully submit that the pending claims are allowable and prompt notification to this effect is respectfully requested.

Respectfully submitted,
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Version marked to show changes made

IN THE SPECIFICATION

The paragraph beginning on page 1, line 14 has been amended as follows:

Different techniques have already been proposed to quantitatively determine the absorption and reduced scattering coefficients of turbid media [media[1]]. See Welch, A.J.; van Gemert, M.J.C., Optical Thermal Response of Laser Irradiated Tissue; Plenum Publishing Corp., New York, 1995, and references therein. Most of the non-invasive methods are based on the measurement of spatially and/or temporally-resolved reflectance. The principle is as follows: the turbid medium is illuminated by a collimated or focused light source. The backscattered light is measured by one or several detectors. Different types of measurements are possible, depending on the time-dependence of the illuminating source: steady-state (continuous source), time-domain (short pulsed source) or frequency domain (amplitude modulated source). The present invention relates to the case of steady-state measurements, performed at different distances ρ between the source and the detectors. However, the technique presented here can be complemented by time- or frequency-domain measurements.

The paragraph beginning on page 2, line 12 has been amended as follows:

1) The first case corresponds to source-detector separations larger than several transport mean free paths. For typical biological tissue optical properties (W.-F. Cheong, S.A. Prahl, and A.J. Welch, "A Review of the Optical Properties of Biological

Tissues," IEEE J. Quantum Electron. 26, 2166-2185 (1990)) [properties[2]], this case corresponds [correspond] to a source-detector separation larger than 2 mm. An analytical form of the reflectance can be obtained from the diffusion equation, if the absorption coefficient μ_a is sufficiently lower than the scattering coefficient μ_s (typically ten times). In such a case, the relevant optical properties are the refractive index, the absorption coefficient and the reduced scattering coefficient. The average depth of probing is on the same order as [than] the source-detector separation ρ.

The paragraph beginning on page 8, line 7 has been amended as follows:

The present definitions are given for clarity of the concepts developed in the patent and are worded in agreement with Welch, A.J.; van Gemert, M.J.C., Optical Thermal Response of Laser Irradiated Tissue; Plenum Publishing Corp., New York, 1995, and references therein [ref.1].

The paragraph beginning on page 11, line 5 has been amended as follows:

The methods described in [the] US Patent 5,517,987 (Tsuchiya) are based on measurements with a large range of source-detector separations, typically from 1 mfp' to 10 mfp'. In such cases, the volume probed is on the order of 10-1000 (mfp')[[3]]. In contrast with such a large scale investigation, the present invention is directed to a novel approach where the volume probed is much smaller, on the order of 1 (mfp')[[3]]. This is achieved by using only small source detector separations, typically from 0.1 to 2 mfp'. The lateral dimension of probing is limited to this range of distances.

The paragraph beginning on page 12, line 5 has been amended as follows:

This is also one result of this simulation to compute the average depth of probing, illustrated in Fig.2.[.] It is demonstrated that only the superficial part of the turbid medium is probed if small source-detector separations are used. For this, we determined the depth below the surface of each scattering event in the simulation. With this information we determined the average depth of all the scattering events for each detected photon, which we present as a probability density function in Fig.2.[.] This figure shows that the average depth of scattering is approximately around 1 mfp'. Moreover it showed that the part located below 2 mfp' <u>was</u> [were] not playing a significant role in the measured signal (for $\rho < 1.5$ mfp').

The paragraph beginning on page 13, line 4 has been amended as follows:

Fig.3 illustrates the fact that the parameter γ is the only predominant parameter of the phase function that must be taken into account (and not $g=g_1$ as frequently mentioned in literature). Different reflectance curves, obtained from Monte Carlo simulations are shown in Fig.3. Four different phase functions were used for the simulations. Three phase functions are characterized by $\gamma=1.25$, but different g_1 and g_2 values. Fig.3[.] shows that almost identical reflectance <u>curves</u> [curve] are obtained for distances $\rho\mu_s'>0.3$, if the g_1 and g_2 are varied in such a way that the parameter γ stays constant ($\gamma=1.25$). For comparison, the reflectance computed with a different g ($=g_1$) value is also presented ($\gamma=2.25$). It appears then clearly that the parameter g ($=g_1$) plays a significant role in the reflectance.

The paragraph beginning on page 15, line 2 has been amended as follows:

In the first embodiment, the [The] apparatus can be divided in three parts, described in Fig.5[.]a.

The paragraph beginning on page 15, line 3 has been amended as follows:

The first part is the illuminating system. Any light source can be used. For example [examples]: a) white sources, such as halogen or xenon lights, metal halides or fluorescent or phosphorescent sources;[.] b) sources such as lasers, laser diodes, optical fiber lasers, light emitting diodes or superluminescent diodes;[.] c) the sources described in points [point] a) and b) where monochromators, filters or interference filters are added to select a given set of wavelengths.

The paragraph beginning on page 15, line 9 has been amended as follows:

In the first preferred embodiment, the [The] light power is conducted to the investigated sample by the probe, which is the second part of the apparatus. The probe is preferably made of optical fibers, to illuminate and to collect the backscattered light. But GRIN rods or other types [type] of light pipes can also be used. Different possible arrangements of optical fibers are illustrated in Fig. 6. [Fig.6 .] Two different modes of measurements can be chosen. First, one fiber is used to illuminate the sample and at least two other fibers are used to collect the backscattered light at two different distances. Second, one fiber is used to collect the light and at least two other fibers, located at two different distances from the first one, are used to illuminate sequentially the sample.

The paragraph beginning on page 16, line 1 has been amended as follows:

The light collected by the probe is analyzed by the detection unit, which is the third part of the apparatus. If wide spectral light sources are used (such as halogen or xenon lights), a spectrograph can be put between the probe and the detector to get wavelength dependence of the backscattered signal (either in the source or detection unit). Any <u>type</u> [types] of <u>detector</u> [detectors] can be used. For example, photodiodes, avalanche photodiodes or photomultipliers can be assigned to each collecting <u>fiber</u> [fibers]. Simultaneous detection of each collecting fiber can also be achieved using linear or two-dimensional detectors such as Charge-Coupled Detectors (1D or 2D), intensified CCD or array of photodiodes.

The paragraph beginning on page 16, line 16 has been amended as follows:

A second type of embodiment is presented <u>in</u> [on] Fig. 5[.]c. The difference with embodiments presented in Fig. 5[.]a[.] and Fig. 5[.]b[.] is that optionally no optical fibers, light pipes or grin rods <u>are</u> [is] used. The light source unit is directly in contact with the turbid medium, as well as the detector unit. Collimating optics, micro-optics or imaging optics (DOE Diffractive Optical Elements for example) can be put between the turbid medium and the actual light sources and detectors. The different type of sources and detectors cited in example for the first embodiment can be used for the second type of embodiments. Hybrid design, such as arrangements involving both direct <u>contact</u> [contacts] sensors or detectors and fibers, light pipes or grin rods are also included in the present embodiment.

The paragraph beginning on page 17, line 5 has been amended as follows:

The third embodiment is described in Fig.5[.]d[.] and Fig.5[.]e. The only difference with the first and second embodiment is that non-contact measurements are performed. A collimating system allows for a point-like illumination on the turbid medium. An imaging system enables the measurement of the spatial distribution of the reflectance. The detectors can be either an array (1D or 2D) of detectors (Fig.5[.]d) with optional scanning 1 and 2 which can operate separately or can be confounded in a single scanner, or a single detector (Fig.5[.]e). In this last case, an scanning device is used to obtain the spatially-resolved reflectance. A fiber bundle, multicore fiber or relay optics (grin rod or multiple lenses) can be put between the focal point of the imaging system and the detector(s). The different type of sources and detectors cited in example for the first embodiment can be used for the third embodiment.

The paragraph beginning on page 17, line 16 has been amended as follows:

Spatial images of the parameters μ_a, μ_s' and γ can be obtained by a series of measurements at different locations, that we call multi-site measurements. Some mechanical or optical scanning device can be used for this purpose. The resolution of such images is on the order of the mean source-detector separation used for a single site measurement. All three embodiments can be expanded to perform multi-site measurements, by duplicating and/or multiplexing the illuminating or measuring devices. For example, the optical fiber probes shown in Fig.6[.], can be duplicated and put side by side. The scanning system described in the third embodiment can also be expanded to perform multi-site measurements.

The paragraph beginning on page 19, line 4 has been amended as follows:

An example of a measurement, after calibration, is shown in Fig.7. The measurement was performed with the apparatus described in the first embodiment, with a probe similar to the one described in Fig.6[.]a. A prior calibration was performed on a solid turbid medium, which optical properties were measured by another technique (frequency domain measurement, <u>cf. Welch, A.J.; van Gemert, M.J.C., Optical Thermal Response of Laser Irradiated Tissue; Plenum Publishing Corp., New York, 1995, and references therein</u> [cf. Ref 1.]). The sample was a water suspension of polystyrene microsphere of 1 μm diameter. The measurement is compared to a Monte Carlo simulation performed with the scattering properties calculated from Mie theory and absorption coefficient of water. <u>Fig.7</u> shows an excellent agreement between the measurement and the simulation, which confirm the validity of our simulation model, experimental measurement and calibration.

The paragraph beginning on page 19, line 16 has been amended as follows:

Artifacts during a measurement, for example due to bad contact between the probe and the sample, or heterogeneity of the sample, can be detected by the following optional procedure. Two illuminating fibers are disposed symmetrically in regard to the collecting fibers (see Fig.6[.]b). If the sample is homogeneous, the reflectance curve should be identical with either illuminating fiber. Therefore, heterogeneity of the investigated region or obstructions beneath the fibers are detected by comparing the two

curves. If the two curves are sufficiently close, the measurement is validated and the average of the two curves is calculated.

IN THE CLAIMS

Claim 5 has been amended as follows:

5. (Twice Amended) The method according to claim 2 [4], wherein [either] the probe is [or the optical and electrical micro-system are] put into contact with [to] the turbid medium.